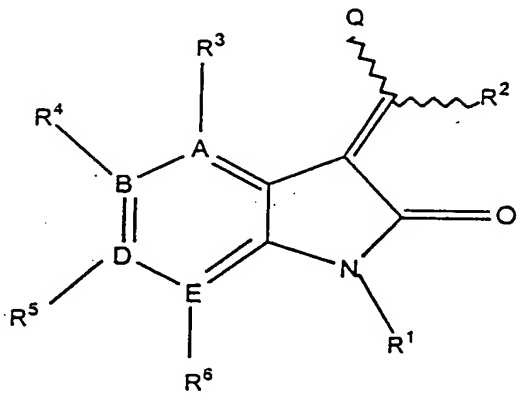
CLAIMS

WHAT IS CLAIMED:

1. A 3-heteroarylidene-2-indolinone having the chemical structure:



or a physiologically acceptable salt or prodrug thereof wherein,

A, B, D and E are selected from the group consisting of carbon and nitrogen, it being understood that the nitrogen-containing 9-member bicyclic ring formed is one known in the chemical arts; it being further understood that when A, B, D, or E is

nitrogen, R^3, R^4, R^5 or R^6, respectively, does not exist;

R^1 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, hydroxy, alkoxy, carboxyl, C-amido and sulfonyl;

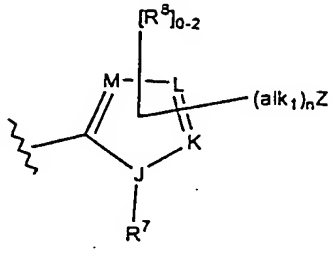
R^2 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, and heteroalicyclic;

R^3, R^4, R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonamido, carbonyl, carboxyl, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino and $-NR^{10}R^{11}$;

R^{10} and R^{11} are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, carbonyl, sulfonyl and, combined, a five- or six-member heteroalicyclic ring containing at least one nitrogen;

R^3 and R^4, R^4 and R^5, or R^4 and R^5 may combine to form a six-member aryl or heteroaryl ring;

Q is a heteroaryl group having the following structure:



J is selected from the group consisting of oxygen, nitrogen and sulfur;

K, L and M are independently selected from the group consisting of carbon, nitrogen, oxygen and sulfur such that the five-member heteroaryl ring formed is one known in the chemical arts, it being understood that when K, L and M are nitrogen, sulfur or oxygen, R^8 or $-(alk_1)_nZ$ cannot be covalently bonded to that atom;

when J is nitrogen, R^7 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, hydroxy, alkoxy, aryloxy, carbonyl, carboxyl, C-amido, guanyl and sulfonyl and when J is

oxygen or sulfur, R^7 does not exist and there is no bond;

R^8 is selected from the group consisting of hydrogen, alkyl, trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, heteroalicyclic, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonamido, carbonyl, carboxyl, cyano, nitro, halo, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, amino, $-NR^{10}R^{11}$, trihalomethyl, a five member cycloalkyl, aryl, heteroaryl or heteoalicyclic ring fused to two adjacent atoms of the Q ring; and a six-member cycloalky, aryl, heteroaryl, or heteroalicyclic ring fused to two adjacent atoms of the Q ring;

R^{10} and R^{11} are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, carbonyl, sulfonyl and, combined, a five- or six-member heteroalicyclic ring containing at least one nitrogen;

alk_1 is selected from the group consisting of optionally substituted methylene (-CRR'-), optionally substituted ethylene (-C(R)=C(R')-) and acetylene (-C≡C-);

R and R' are independently selected from the group consisting

of hydrogen, alkyl, cycloalkyl, aryl, alkoxy, thioalkoxy, aryloxy and halo;

n is 0 to 10, inclusive; and

Z is a polar group.

2. The compound, salt or prodrug of claim 1 wherein,

K, L and M are carbon;

R^8 is selected from the group consisting of hydrogen, alkyl, halo, cyano, carboxyl, a six-member cycloalkyl group fused to 2 adjacent atoms of the Q ring and a six-member heteroalicyclic ring fused to 2 adjacent atoms of the Q ring;

alk_1 is selected from the group consisting of CH_2 and CH_2CH_2;

n is 0, 1, 2 or 3; and,

Z is selected from the group consisting of hydroxy, alkoxy, amino, carboxyl, carbamyl, amido, morpholino, piperazinyl, tetrazolo, sulfonyl, sulfonamido, ureido and phosphonyl.

3. The compound, salt or prodrug of claim 2 wherein, J is nitrogen.

4. The compound, salt or prodrug of claim 2 wherein, J is sulfur.

5. The compound, salt or prodrug of claim 2 wherein, J is oxygen.

6. The compound, salt or prodrug of claim 3 wherein, R^7 is hydrogen.

7. The compound, salt or prodrug of claim 2 wherein,

A, B, D and E are carbon;

R^3, R^4, R^5 and R^6 are independently selected from the group consisting of hydrogen, alkyl, trihaloalkyl, alkoxy, halo, amino and $-NR^{10}R^{11}$; and,

R^{10} and R^{11} are independently selected from the group consisting of hydrogen, alkyl, carbonyl and sulfonyl.

8. The compound, salt or prodrug of claim 7 wherein, R^1 is hydrogen.

9. The compound, salt or prodrug of claim 1 wherein,

A, B, D and E are carbon;

J and L are nitrogen;

R^7 is selected from the group consisting of:

unsubstituted lower alkyl;

unsubstituted aryl;

unsubstituted heteroaryl;

unsubstituted heteroalicyclic;

sulfonyl;

unsubstituted lower alkoxy;

trihalomethanesulfonyl;

aryl substituted with one of more groups independently selected from the group consisting of:

halo;

amino;

hydroxy;

cyano;

unsubstituted lower alkyl;

unsubstituted lower alkoxy;

carboxyl;

S-sulfonamido;

lower alkyl substituted with one or more groups selected from the group consisting of:

halo;

hydroxy;

amino;

carboxyl; or,

lower alkoxy substituted with one or more halo groups;

heteroaryl substituted with one or more groups independently selected from the group consisting of:

halo;

amino;

hydroxy;

cyano;

unsubstituted lower alkyl;

unsubstituted lower alkoxy;

carboxyl;

S-sulfonamido;

lower alkyl substituted with one or more groups

selected from the group consisting of:

halo;

hydroxy;

amino;

carboxyl; or,

lower alkoxy substituted with one or more halo groups;

R^8 is selected from the group consisting of:

unsubstituted lower alkyl;

lower alkyl substituted with one or more groups selected from the group consisting of:

halo;

hydroxyl;

unsubstituted lower alkoxy;

amino; or,

carboxyl;

unsubstituted lower alkoxy:

lower alkoxy substituted with one or more halo groups;

unsubstituted aryl;

unsubstituted heteroaryl

unsubstituted heteroalicyclic

aryl substituted with one or more groups independently selected from the group consisting of:

halogen;

hydroxy;

carboxyl;

nitro;

cyano;

amino;

$-NR^{10}R^{11}$;

S-sulfonamido;

unsubstituted lower alkoxy;

lower alkoxy substituted with one or more halogens;

unsubstituted lower alkyl;

lower alkyl substituted with one or more groups selected from the group consisting of:

halogen;

hydroxy;

amino;

$-NR^{10}R^{11}$; or,

carboxyl

heteroaryl substituted with one or more groups independently selected from the group consisting of:

halogen;

hydroxy;

carboxyl;

nitro;

cyano;

amino;

$-NR^{10}R^{11}$;

S-sulfonamido;

unsubstituted lower alkoxy;

lower alkoxy substituted with one or more halogens;

unsubstituted lower alkyl;

lower alkyl substituted with one or more groups selected from the group consisting of:

halogen;

hydroxy;

amino;

$-NR^{10}R^{11}$; or,

carboxyl

heteroalicyclic substituted with one or more groups independently selected from the group consisting of:

halogen;

hydroxy;

carboxyl;

nitro;

cyano;

amino;

$-NR^{10}R^{11}$;

S-sulfonamido;

unsubstituted lower alkoxy;

lower alkoxy substituted with one or more halogens;

unsubstituted lower alkyl;

lower alkyl substituted with one or more groups selected from the group consisting of:

halogen;

hydroxy;

amino;

$-NR^{10}R^{11}$; or,

carboxyl; and,

R^3, R^4, R^5 and R^6 are independently selected from the groups consisting of hydrogen, halogen, nitro, amino, cyano, S-sulfonamido, carboxyl, trihalomethyl, unsubstituted lower alkyl and lower alkyl substituted with one or more groups selected from the group consisting of halogen, hydroxyl, carboxyl, unsubstituted lower alkoxy and lower alkoxy substituted with one or more halo groups.

10. A method for the modulation of the catalytic activity of a protein kinase comprising contacting said protein kinase with said compound, salt or prodrug of any one of claims 1

through 9.

11. The method of claim 10 wherein said protein kinase comprises a protein tyrosine kinase.

12. The method of claim 11 wherein said protein tyrosine kinase comprises a receptor protein tyrosine kinase.

13. The method of claim 12 wherein said receptor protein tyrosine kinase is selected from the group consisting of EGF, HER2, HER3, HER4, IR, IGF-1R, IRR, PDGFRα, PDGFRβ, CSFIR, C-Kit, C-fms, Flk-1R, Flk4, KDR/Flk-1, Flt-1, FGFR-1R, FGFR-2R, FGFR-3R and FGFR-4R.

14. The method of claim 11 wherein said protein tyrosine kinase comprises a non-receptor protein tyrosine kinase.

15. The method of claim 14 wherein said non-receptor protein tyrosine kinase is selected from the group consisting of Src, Frk, Btk, Csk, Abl, ZAP70, Fes/Fps, Fak, Jak, Ack, Yes, Fyn, Lyn, Lck, Blk, Hck, Fgr and Yrk.

16. The method of claim 10 wherein said protein kinase comprises a serine-threonine protein kinase.

17. The method of claim 16 wherein said serine-threonine protein kinase is selected from the group consisting of CDK2 and Raf.

18. A pharmacological composition of said compound, salt or prodrug of any one of claims 1 through 9.

19. A method for treating or preventing a protein kinase related disorder in an organism comprising administering a therapeutically effective amount of said pharmacological composition of claim 18 to said organism.

20. The method of claim 19 wherein said protein kinase related disorder comprises a receptor protein tyrosine kinase related disorder.

21. The method of claim 20 wherein said receptor tyrosine kinase related disorder comprises an EGFR related disorder.

22. The method of claim 21 wherein said EGFR related disorder is a cancer selected from the group consisting of squamous cell carcinoma, astrocytoma, glioblastoma, lung cancer, bladder cancer, head and neck cancer.

23. The method of claim 20 wherein said receptor protein tyrosine kinase related disorder comprises a PDGFR related disorder.

24. The method of claim 23 wherein said PDGFR related disorder is a cancer selected from the group consisting of glioblastoma, melanoma, lung cancer, ovarian cancer or prostate cancer.

25. The method of claim 20 wherein said receptor protein tyrosine kinase related disorder comprises an IGFR related disorder.

26. The method of claim 25 wherein said IGFR related disorder is a cancer selected from the group consisting of breast cancer, small-cell lung cancer or glioma.

27. The method of claim 26 wherein said IGFR related

disorder comprises diabetes.

28. The method of claim 20 wherein said protein tyrosine kinase related disorder comprises a flk related disorder.

29. The method of claim 28 wherein said flk related disorder is a cancer selected from the group consisting of breast cancer, ovarian cancer, lung carcinoma and glioblastoma.

30. The method of claim 19 wherein said protein kinase related disorder comprises a serine-threonine kinase related disorder.

31. The method of claim 30 wherein said serine-threonine kinase related disorder comprises an autoimmune disorder.

32. The method of claim 31 wherein said serine-threonine kinase related disorder comprises a hyper-proliferation disorder.

33. The method of claim 632 wherein said hyper-

proliferation disorder is selected from the group consisting of restinosis, fibrosis, psoriasis, osteoarthritis and rheumatoid arthritis.

34. The method of claim 19 wherein said protein kinase related disorder comprises an inflammatory disorder.

635. The method of claim 19 wherein said protein kinase related disorder comprises angiogenesis.

36. The method of claim 19 wherein said organism is a mammal.

37. The method of claim 36 wherein said mammal is a human.